1960 ANNUAL REPORT

VIRUS REFERENCE LABORATORY*

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During 1960 the following have contributed to the work of the virus reference laboratory: J. H. Connolly, M.D.; J. R. L. Forsyth, M.B.; D. H. Simpson, M.B.; M. Haire, M.B.; J. K. Clarke, B.Sc.; D. S. Dane, M.B., and G. W. A. Dick, M.D.; J. Evans, J. Cummings, and J. J. McAlister, F.I.M.L.T.

THE Virus Reference Laboratory has now been in operation for four years and it seems a suitable time to consider what types of investigation have proved to be most valuable, so that in the future the work of the laboratory will not be dissipated in unrewarding investigations, but can be channelled in the directions where it will be most useful to the community.

It must be appreciated that a virus reference laboratory is *not* the virological equivalent of a routine diagnostic bacteriology laboratory. The reason for this is that at the present time, with the exception of poliomyelitis and a few other virus infections, the available diagnostic techniques cannot provide a laboratory diagnosis with the same speed as can be provided for many bacterial infections. Thus, frequently a virological diagnosis can only be made when it is too late to influence the course of treatment. There is only one group of viruses (Lymphogranuloma venereum and Trachoma) which are known to produce chronic infections, and with other chronic infections it is most unlikely that the virus reference laboratory can be of any help. The often time-consuming investigation of an isolated illness of supposed viral ætiology has seldom been rewarding to the clinician or the virologist. The function of a virus reference laboratory is to undertake special investigations rather than routine diagnostic work, and in our experience it has been the special investigations that have given the most useful results.

The types of investigation which have in the past been valuable and on which we consider the Virus Reference Laboratory should devote most effort are as follows:—

(a) The diagnosis of all cases of poliomyelitis, encephalitis, and aseptic meningitis.

(b) The surveillance of poliomyelitis vaccination, the evaluation of the safety and effectiveness of other viral vaccines, such as influenza vaccine, and the provision of information necessary for planning and assessing measures for the prevention and control of virus diseases.

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(c) To provide early warning or rapid confirmation of possible outbreaks or importations of virus infection, e.g., in such enterprises as the World Health Organization influenza spotting scheme and in the diagnosis of suspected cases of smallpox.

(d) To assist in special studies, e.g., the Medical Research Council chronic bronchitis trial and other special investigations, such as viral myocarditis, in collaboration with clinicians.

Poliomyelitis.

Laboratory Diagnosis of Notified Cases.

During 1960 there were fifteen notifications of poliomyelitis cases in Northern Ireland, of whom eleven were paralysed. One of the paralysed patients died. Revised diagnoses of scurvy, staphylococcal meningitis, tonsillitis or Coxsackie B_5 aseptic meningitis were made in the four notified non-paralytic infections. The viruses isolated from these notified cases are shown below.

Viruses recovered from Patients notified as Suffering from Poliomyelitis.

Notified	Number of Cases	Number Immunized	Viruses Isolated: Polio Type I	Polio Type II	Polio Type III	Coxsackie B_5	Untyped Entero-Viruses	Total Viruses Isolated
Paralysed	11*	0	4	–	6	–	1	11
Not Paralysed	4	2	–	–	–	1	–	1

*Includes one death.

It will be seen that there was one paralysed individual (a baby of 6 months) from whom an unidentified enterovirus was isolated.

The four type I paralytic infections occurred in the first quarter of the year, and with one exception came from the Belfast area. The type III infections were all from the Newry area except for a 34-year-old adult who was infected and became paralysed in Eire. The ages of the paralysed individuals from whom polioviruses were isolated were as follows:

Years	0–1	1	2	3	4	5	34
Number	1	4	1	0	2	1	1

In addition to these virologically confirmed cases there was serological evidence suggesting that a type II virus may have been responsible for wasting of the right calf and buttocks of a 4-year-old boy who had an undiagnosed illness in November, 1959.

Asymptomatic infections.

Two type I viruses and one type III virus were isolated from contacts of paralytic cases, and two type I viruses from asymptomatic infections.

Vaccine surveillance.

As in previous years efforts were made to follow up all diagnosed cases and to obtain information on their poliomyelitis vaccination status and their history of recent injections, etc. *None of the individuals paralysed during 1960 had received any immunization against poliomyelitis.* In none of them was there any history of other inoculations which might have suggested provocation paralysis.

The ages of the paralysed patients, all of whom, except the adult from Eire, were 5 years old or under stresses the risk of paralytic polio in pre-schoolchildren in Northern Ireland and the importance of paying particular attention to the immunization of this age group.

Epidemiology of type III outbreak in Newry area.

Since 1958 no type III poliovirus has been isolated in Northern Ireland. On 23rd July, 1960, a boy aged 4 years travelled from Coventry to Newry. He was ill during the journey and the following day he was paralysed. He was admitted to hospital on 25th July with paralysis of all limbs and was shown to be infected with type III poliovirus. As so commonly happens when there is a hospitalized child in a family, his sister, aged 3 years, stayed with friends in another part of Newry while the mother was visiting the hospital. The sister, although showing no signs of illness, was also excreting type III virus and a second paralytic case due to type III virus occurred in an 18-months-old baby living in the street where the sister had stayed. The brother of this baby was in the habit of visiting an aunt at Bessbrook, and on 21st September a child of $4\frac{1}{2}$ years living there became paralysed with type III virus. The siblings of the Bessbrook child played with a family in Camlough, one of whom, a child of 18 months, became paralysed on 18th October; again type III virus was isolated. A fifth case in a $2\frac{1}{2}$-year-old child due to type III virus occurred at Cladybeg, eight miles from Camlough, on 17th December.

It is clear that the type III virus was imported from England and spread slowly in the area, resulting in the paralysis of four other children. It is reasonable to assume that if the sister of the first paralysed child had been quarantined to house and garden, four paralytic cases would have been prevented.

Outbreak control in 1961.

There seems little doubt that within the next few years epidemics of poliomyelitis will cease in countries where there are *high* rates of immunization with poliovirus vaccines. It may well be that in vaccinated communities polioviruses will virtually disappear as had occurred with *C. diphtheria* in well-immunized populations. However, it also seems likely that, as with diphtheria, cases will continue to occur from time to time as a result of "importations" of virus from elsewhere. There is increasing evidence in favour of the "narrow stream" spread of epidemic poliomyelitis where the source of infection of the paralytic cases can be traced to direct contact with other paralytic cases or their immediate contacts. It seems reasonable, therefore, that attempts should now be made to

see whether the spread of poliovirus can be restricted by using measures similar to those adopted for the control of diphtheria and smallpox.

In consultation with Medical Officers of Health and the Ministry of Health it has been decided to institute immediately the following measures on the clinical diagnosis of a case of paralytic poliomyelitis.

(1) Immediate quarantine of the patient.

(2) House and garden quarantine of siblings and close familial child contacts.

(3) Immunization of contacts who have not been immunized, or who are inadequately immunized, with high potency inactive virus vaccine.

(4) The distribution of a pamphlet explaining about the spread and prevention of poliomyelitis and the importance of minor illnesses, etc. (Appendix I).

(5) Immunization and boosting where necessary of children in the periphery of the area where the case has occurred with the vaccines in routine use.

The effectiveness of these measures on the control of spread of the virus will be studied by the laboratory. Whether or not they can be successful will depend on (a) the physician *immediately* informing the Medical Officer of Health when a case is diagnosed clinically and (b) on the rapidity with which the outbreak prevention methods are brought into operation.

Survey of poliovirus antibody in Co. Down children.

In order to provide information on whether a fourth dose of inactivated poliovirus vaccine was necessary and also to obtain an index of the immune status of the child population for future comparative studies, an immunological survey was made in Co. Down in the summer of 1960. The results of the survey in the under-16-year-old population of whom 95 per cent. had received three doses of vaccine may be summarized as follows:

(a) Ninety-nine per cent. of the children had antibody to type II virus and 94 per cent. to type III virus.

(b) Immunity to type I virus which causes most paralysis was less satisfactory in the 1 to 5 year age group, for only 72 per cent. of these children had antibody to this virus compared with 98 per cent. of older children.

(c) In the 1 to 5 year age group it was found that 94 per cent. of children tested within a year after receiving the third dose of vaccine had antibody to type I virus, but only 64 per cent. of children of this age group tested more than one year after the third dose had antibody.

It may be concluded from these studies that a fourth dose of vaccine is desirable for the younger children in Northern Ireland about one year after the third dose in order to boost their immunity to type I virus. The results of this study will be published in detail elsewhere (Dane and Dick, in press).

Aseptic meningitis.

In forty-eight patients with aseptic meningitis, mumps virus was the causative agent in four and the following enteroviruses were isolated from the others:

Coxsackie B_5		Other Enteroviruses		Total
28	...	16	...	44

The mumps virus infections were diagnosed serologically, and in one of these infections Coxsackie B_5 virus was also present. The commonest cause of aseptic meningitis during 1960 was Coxsackie B_5 virus. This is in contrast to 1959 when there was no evidence of any marked prevalence of any particular enterovirus, and to 1958 and 1957 when mumps and type I poliovirus were respectively the most important causes of aseptic meningitis. It is noteworthy that not a single case of aseptic meningitis during 1960 was due to poliovirus.

Coxsackie Infections.

Coxsackie B_5 virus.

During 1960 there were many infections with Coxsackie B_5 virus in the United Kingdom. In Northern Ireland Coxsackie B_5 virus was isolated from many asymptomatic patients and was found to be associated with the following illnesses:

Aseptic meningitis	28
Bornholm disease	16
"Flu"-like illness	9
Respiratory infection	3

While there is little doubt about this virus being the cause of Bornholm disease and aseptic meningitis during 1960, it is less certain that it was responsible for the "flu"-like illnesses and other respiratory infections, for it is possible that in some of these illnesses Coxsackie B_5 was merely a fellow-traveller.

The best evidence for the implication of an enterovirus as the cause of a particular illness is usually found in outbreaks of disease such as occurred in a boys' school during 1960. During June and July fifty-one boys in a preparatory boarding school became ill. Unfortunately we did not hear of this outbreak until towards the end of the epidemic when nineteen boys were found to be excreting Coxsackie B_5 virus in their fæces.

The symptoms and signs of illness in these nineteen boys were:

Signs and Symptoms	No.
Pyrexia and malaise	19
Headache	18
Pharyngitis	13
Nausea	10
Chest pain	9
Vomiting	8
Abdominal pain	6
Backache	3
Neck stiffness	3
Dizziness	2

Six had relapses after apparent recovery, with recrudescence of symptoms and signs. One boy had electrocardiographic evidence of myocarditis for nine weeks (Connolly, 1961) and another boy was admitted to hospital with a diagnosis of meningitis. Convalescence after these Coxsackie B_5 infections was characterized by marked lassitude, but in all cases recovery was complete.

Coxsackie B_5 virus was isolated from three contacts of ill patients, from one patient with appendicitis and from forty-nine fæcal samples collected from 888 children admitted to the Royal Belfast Hospital for Sick Children, and from one healthy baby. A review of the case histories of the children from whom this virus was isolated provided the following diagnoses:

Respiratory illness - - - -	28
Meningitis - - - - -	3
Vomiting and abdominal pain - - -	4
Miscellaneous - - - - -	14

In many cases the clinical conditions for which they were admitted could have been caused by this virus.

Coxsackie B_1 virus.

In two patients with cardiac symptoms there was serological evidence of infection with Coxsackie B_1 virus. One of these was a man of 53 years who had clinical and electrocardiographic evidence of pericarditis; his electrocardiograph remained abnormal for at least three months after infection. The other patient was a woman of 37 years who had Bornholm disease which symptomatically resembled coronary occlusion. Her electrocardiograph was normal.

Other Enterovirus Investigations.

Investigation in Babies.

A preliminary investigation of the enteroviral flora of the infant gut was made in babies born at the Royal Maternity Hospital. An attempt was made to obtain a weekly fæcal specimen from these babies during the first year of life and to test the specimens for enteroviruses. Of thirteen babies born between April, 1959, and January, 1960, from whom *regular* weekly fæcal samples were obtained, ten were found to be excreting virus at one time or another. Forty-three viruses were isolated, including a type I poliovirus and a Coxsackie B_5 virus. There was no evidence of a seasonal incidence of virus infection nor was infection related to any particular period in the first year of life in this small sample. Three of the babies were excreting virus within 9, 15, and 23 days of birth respectively.

Samples from children admitted to the Royal Belfast Hospital for Sick Children.

In an attempt to obtain some index of the polioviruses circulating in the community, fæcal specimens were collected from 888 children admitted to the Royal Belfast Hospital for Sick Children. Only one type I poliovirus was isolated from an asymptomatic carrier. Although the sampling of this population was not as complete as had been hoped for when the study commenced, the single

positive specimen did not indicate a wide dissemination of poliovirus. In contrast to the single isolate of poliovirus a total of 139 other enteroviruses were isolated.

Respiratory Viruses.

Influenza.

As part of the World Health Organization influenza-spotting scheme, the laboratory continued attempts to detect the presence of influenza virus in the community. This scheme depends entirely on the collaboration of general practitioners. Although the coverage during 1960 was less satisfactory than in previous years, there was little evidence of influenza virus in the community during 1960. In March and April serological evidence of infection with influenza A virus was obtained in two patients, one of whom had a staphylococcal pneumonia and the other "pleurisy." In May a strain of Asian virus was isolated from an adult male with influenza. During the autumn and early winter there was no evidence of influenza virus in the community preceding the explosive outbreak at the beginning of 1961.

Medical Research Council chronic bronchitis trial.

In collaboration with Dr. Eileen O. Bartley and the Department of Therapeutics specimens collected from patients under study in the Medical Research Council chronic bronchitis trial are being examined for viruses.

Respiratory viruses in children.

An investigation of the viral ætiology of 117 respiratory infections in children was made in collaboration with Professor F. M. B. Allen. Although this study provided experience with techniques required for the study of some of the more recently isolated respiratory viruses, it has been unrewarding to the clinicians and virologists. No adeno- or *para-influenza* viruses were isolated from these children, but serological evidence of recent adenovirus infection was found in three children with pneumonia and in three other children with pneumonia there was evidence of recent infection with para-influenza 3 virus. A number of enteroviruses (four Coxsackie group B virus and two Echo viruses) were isolated from children with respiratory illnesses. While certain of the enteroviruses have been associated with respiratory illnesses, in the absence of an epidemic of respiratory infection associated with one or other type of enterovirus their ætiological importance remains uncertain.

The association of para-influenza viruses and adenoviruses with pneumonia in children requires further investigation, and most information will be obtained from virological investigation of outbreaks or a series of cases, rather than of isolated respiratory illnesses.

Special Investigations.

Rickettsioses and multiple sclerosis.

LeGac, Giroud, and Dumas (1960) have claimed that cases of multiple sclerosis have an epidemiological pattern and histological lesions similar to that of rickettsial infections. Although there is no evidence of Q fever (Murray, Dane, and Dick, 1958) or other rickettsial infections in Northern Ireland and no evidence of any similarity of the histological lesions of rickettsioses and fatal multiple sclerosis

cases in Northern Ireland (Professor J. H. Biggart, personal communication), the Virus Reference Laboratory was requested to carry out some tests for Q fever antibody in the sera of patients with a clinical diagnosis of multiple sclerosis.

Sera from thirty patients with multiple sclerosis were tested for complement fixing antibody to the Nine mile strain of *Rickettsia burnetii*. Of these sera twenty-seven were negative at a dilution of 1 : 4 and the remaining three were anticomplementary. There is thus no evidence of an association of *R. burnetii* infection and multiple sclerosis in Northern Ireland.

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POLIOMYELITIS

ADVICE TO PARENTS

THIS NOTICE IS SENT TO YOU BECAUSE A CASE OF POLIOMYELITIS HAS OCCURRED IN YOUR NEIGHBOURHOOD.

Poliomyelitis is an infectious disease that spreads from person to person, and it may be spread by people who are not themselves ill. It is most unlikely that you or any of your family will become ill, but you can do several things to make this even less likely and to assist in measures to prevent the disease spreading.

These are the rules we would like you to follow:

1. Make quite sure that you and your family have been properly immunized against poliomyelitis. If in doubt ask your doctor or health visitor about this. Arrangements are now being made to immunize all those who need it.

2. Wash your hands after going to the lavatory and see that your children do this too. Also wash your hands before preparing food.

3. Avoid kissing small children outside your own family and do not let your children visit or play with other children who are unwell themselves or have a brother or sister who is ill.

4. Avoid crowds and do not travel unnecessarily with children.

5. If anyone in your household is off-colour or ill make sure they stay at home and go to bed and that you inform your doctor immediately. Do not allow visitors, particularly other children.

Don't forget about immunization, but remember that it is a few days before it can give any protection and therefore it needs to be done as soon as possible.

Don't be alarmed. Very few of the people who get infected with the poliomyelitis virus become ill, and of the few who do become ill many recover completely. You have been sent this notice because if you and everyone else follow the rules outlined above we can prevent some cases of poliomyelitis.